Optical Projection Tomography as a quantitative 3D validation technique for MRI of labeled pancreatic islets

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Introduction

Islets graft transplantation has emerged as a potential strategy for treatment of diabetes but is hampered by progressive islet loss [1]. The quantification of pancreas islets (PIs) help assess islets graft loss post transplantation. MRI of PIs labeled with iron oxide particles is the most promising (high spatial resolution, capacity for longitudinal assessment) approach [2]. However, it is challenged by the false positive hypointense signal intensity (blood vessels etc.). Alternatively, optical projection tomography (OPT) provides high resolution 3D images for non-fluorescent specimens and allows multi-spectral staining for different tissues/cell types [2, 3]. Here, our objective is to cross-validate the labeled PIs as observed in the OPT & MRI.

Methods

Pancreatic islets were isolated from mice and labeled with micron-sized iron oxide (MPIOs) particles (ME04F, diameter 1-1.99 µm, BangsLab). Labeled PIs were injected into pancreatic lobes, fixed and mounted in agarose. Two sequential scans (pancreatic tissue, labeled islets) were performed on a Biophotonics 3001 OPT scanner (Bioptonics). MRI (3D T_2*-weighted gradient echo MRI (FLASH) was performed on a 9.4T Biospec small animal MRI scanner (Bruker Biospec). In order to co-localize the labeled islets in OPT and MR images, the OPT image was co-registered to MR image, using [4]. For quantitative assessment, we segmented the (connected) voxel clusters from individual modalities, as well as those which were co-localized.

Results

Qualitative visualization and quantitative measures of PI's from OPT/MRI were reported for two representative phantoms A and B (see Figure, Table). The 3D rendering of pancreatic tissue, is overlaid with cluster of voxels segmented from MRI (hypointense, in red) and OPT channel (islets channel, in green, co-localized in yellow). Quantification revealed 90% agreement of OPT signals with corresponding MRI signals. Approximately 85% of MRI signals did not overlap with an OPT signal, indicating large numbers of false positive signals in FLASH MR images. The accuracy of OPT/MRI co-registration were qualitatively assessed and deemed appreciable.

Conclusions

Successful co-registration of PIs from MRI and OPT allowed cross-validation of MR images, confirming its suitability for *in vivo* PI imaging. This is an essential prerequisite for future validation of *in vivo* MRI data using beta-cell targeting iron oxide based nanoparticles. While the clusters correspond between OPT/MRI, the large number of false positives in MRI is likely explained by air bubbles resulting from the phantom preparation, which is not an issue for future *in vivo* assessments.

Acknowledgement / References

This work was supported by the EC FP7 MC ITN BETATRAIN. **Refereces:** (1) Gavin Low, 2010.; (2) T. Alanentalo, et al. 2007; (3) A. Hörnblad, 2011. (4) F Maes, et.al. 1997.

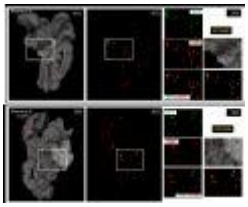
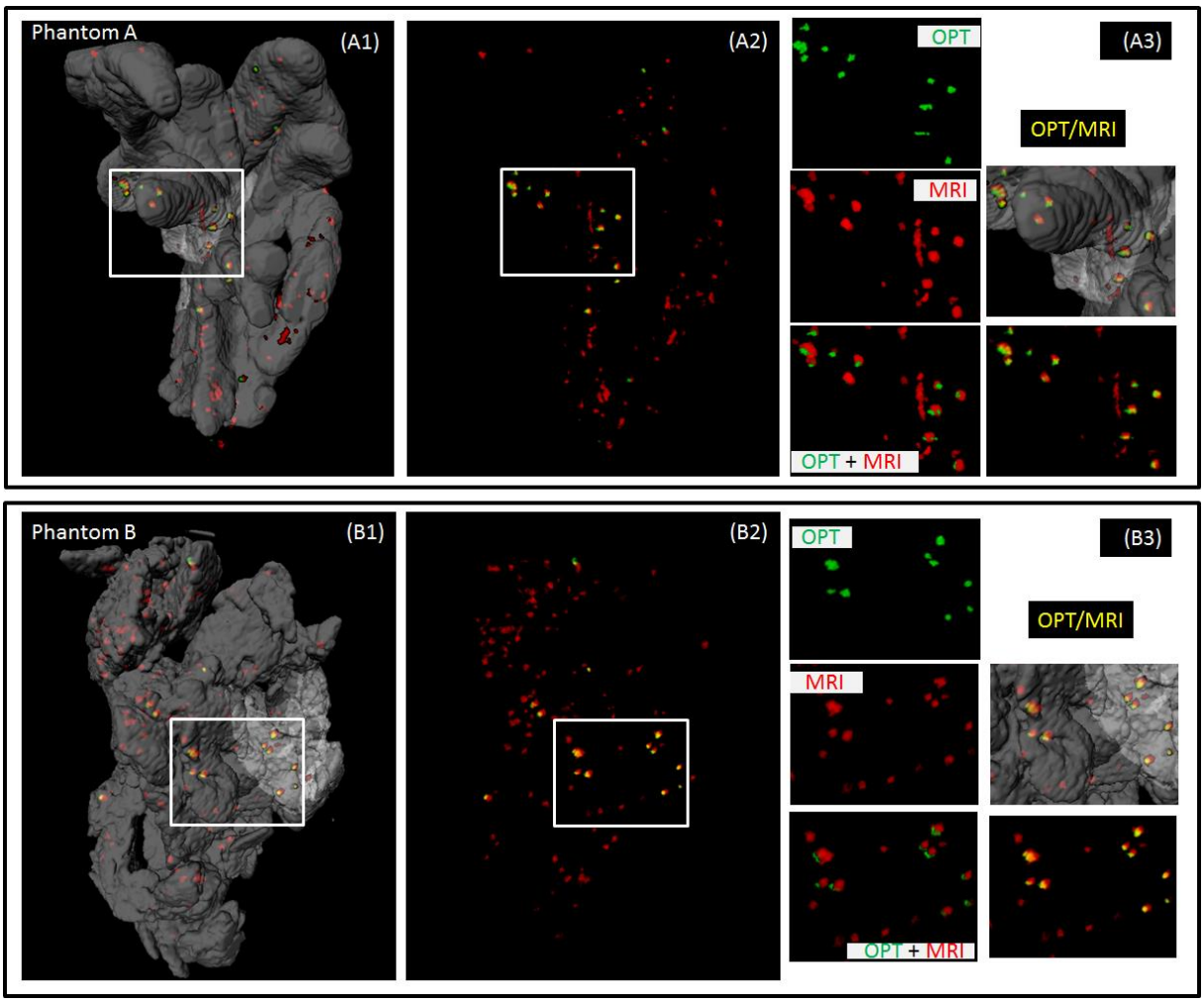


Figure 1:
Co-localization of pancreatic islets in OPT (green),MRI (red). Overlay (yellow)

Table 1:
Quantitative measure of PI clusters in OPT and MR images



	Total MPIOs	OPT MPIOs within ROI	MRI clusters within ROI	Co-localized	False -ve	False +ve
Phantom A	21	20	107	18	2	89
Phantom B	22	16	122	15	1	107